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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,703	KOPRESKI, MICHAEL S.	
	Examiner	Art Unit	
	Meera Natarajan	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-9,16,17,21,22,24,26 and 28-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-15,18-20, 23,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III, Claims 10-15, 18-20, 23, 25 and 27 in the reply filed on 07/20/2007 is acknowledged. The traversal is on the ground(s) that "the cited reference in the restriction requirement does not impinge on the unity of the invention in these claims". This is not found persuasive because as stated in the restriction requirement mailed 06/29/2007, Claim 1 recites a method for extracting, isolating, or concentrating an apoptotic body present in a bodily fluid. In view of this Reutelingsperger et al. teach a method of extracting apoptotic cells from a blood sample of a cancer patient (see Example 3) using annexin V as a probe. As defined in the specification "apoptotic bodies are or comprise cellular fragments released, shed, or extruded from a cell during apoptosis" (see p.1 of the instant specification lines 18-20) and the disclosure of Reutilingsperger states the final stage of apoptosis is the cell breaks up into a number of small apoptotic bodies (see column 1, paragraph 4, last sentence). Therefore the technical feature recited in Claim 1 is not special and the groups are not so linked as to form a single general concept under PCT Rule 13.1. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-9, 16-17, 21, 22, 24, 26, 28-36 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/20/2007.

3. The species election of "fluorescent" for the label, "microwave" for the disruption method, and "mass spectrometry" for the detection method is acknowledged. After further consideration the species election for disruption method and detection method has been extended. The disruption method will include "chemical" and the detection method will include "flow cytometry".

4. Claims 10-15, 18-20, 23, 25 and 27 will be examined on the merits.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 10-11, 16, 18, 19, and 23 rejected under 35 U.S.C. 102(b) as being anticipated by Homburg et al. (Blood Vol. 85(2), pp.532-540 January 1995).

7. The Claims are drawn to method of detecting a protein or phospholipid of an apoptotic body in serum from a patient, the method comprising extracting, separating, isolating or purifying the protein or phospholipid of the apoptotic body from serum, labeling the protein or phospholipid of the apoptotic body and detecting the labeled protein or phospholipid of the apoptotic bodies using fluorescent labeled probes/beads and flow cytometry.

8. Homburg et al. teach neutrophils shed their surface Fc gamma RIII during apoptosis in vitro. The Fc gamma RIII-negative subpopulation exhibited typical morphological changes, such as nuclear condensation and DNA fragmentation.

Furthermore, this subpopulation appeared to have acquired the property of binding phospholipid Annexin V. The property of Annexin V binding was not shared by the nonapoptotic Fc gamma RIII-positive subpopulation. Homburg et al. results indicate that soluble Fc gamma RIII in body fluids might be derived for a large part from neutrophils undergoing apoptosis in tissues (see Abstract). Neutrophils were obtained from blood samples from healthy volunteers and sorted by FACS analysis and flow cytometry (see Materials and Methods p. 533, left column – p.534 and 535 top right column) for apoptotic cells (apoptotic bodies with nuclear condensation) (see Figure 6 and 7). Soluble Fc gamma RIII protein was detected in a culture of isolated apoptotic cells using a radioimmunoassay with sepharose beads (see Materials and Methods, p. 534, right column last paragraph). Annexin V phospholipid was detected using FITC labeling and flow cytometry (see fig. 3). Therefore Hamburg et al. teach isolating apoptotic neutrophils (which form apoptotic bodies) from a blood sample and detecting protein (Fc gamma RIII) or phospholipid (Annexin V) using fluorescent labeled probes/beads and flow cytometry.

9. Claims 10-14, 23, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Jahr et al. (Cancer Research Vol. 61, pp.1659-1665, February 2001).

10. The Claims are drawn to a method of detecting a nucleic acid of an apoptotic body in serum from a cancer patient, the method comprising extracting, separating, isolating or purifying the nucleic acid of the apoptotic body from serum, labeling the nucleic acid of the apoptotic body or its amplified product using a labeled primer or

probe specific for a nucleic acid of the apoptotic body and detecting the labeled nucleic acids of the apoptotic bodies using flow cytometry and wherein the presence of the nucleic acids of the apoptotic bodies in the serum is associated with a cancer or a premalignant condition.

11. Jahr et al. teach the presence of DNA fragments in the blood plasma of cancer patients and evidence of their origin from apoptotic and necrotic cells. The specification discloses "apoptotic bodies are or comprise cellular fragments released, shed, or extruded from a cell during apoptosis" (see p.1 of the instant specification lines 18-20). Therefore as evidence by the specification the DNA fragments identified from apoptotic cells taught by Jahr et al. are essentially nucleic acids of "apoptotic bodies". Jahr et al. teach extracting, separating, and isolating nucleic acids of apoptotic bodies from plasma samples obtained from cancer patients. The DNA was extracted and isolated using Qiagen kits, that are well known in the art to use chemical disruption, and detected using fluorescently labeled primers and probes and quantitative PCR and gel electrophoresis (see materials and methods p. 1659-1660). "The results of quantitation revealed a wide spectrum of DNA concentrations in the plasma of cancer patients, between 10 and 1200 ng/ml (see p. 1660, last sentence right column). Thus, we conclude that elevated levels of circulating DNA appear to be a characteristic feature of most, but not all of the carcinoma diseases" (see p. 1661, top right column). Jahr et al. further teach that the circulating DNA in the plasma of cancer patients originate from apoptotic cells. Jahr et al. state "Our studies with cell cultures and animal models show that soluble DNA in the form of chromatin fragments are released from apoptotic and

necrotic cells and can eventually appear in the blood stream. We, therefore, assume that the source of DNA in the blood plasma of cancer patients are cells that disintegrate by apoptosis and/or necrosis in expanding tumor tissue" (see p. 1664, last paragraph left column through top right column). Therefore the reference teaches each and every limitation of the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 15 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jahr et al. (Cancer Research Vol. 61, pp.1659-1665, February 2001) in view of Mok et al. (J. Natl. Cancer Inst. Vol. 93(9), pp.1458-1464 Oct. 2001).

15. The Claims are drawn to the method of Claim 10 wherein the nucleic acid is extracted from the apoptotic body and hybridized to a solid substrate such as a bioelectric interface.

16. The teaches of Jahr et al. are presented in the 102(b) rejection set forth above. Jahr et al. does not teach hybridizing the extracted nucleic acid to a bioelectric interface. This deficiency is made up for in Mok et al.

17. Mok et al. teach identification of potential serum markers in ovarian cancer using microarray technology. RNA was isolated and pooled from three ovarian cancer cell lines and from three normal human ovarian surface epithelial cells lines. Complementary DNA generated from these pools was hybridized to a microarray slide and genes overexpressed in the cancer cells were identified (see Abstract).

18. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the technique taught by Mok et al. to identify nucleic acids of apoptotic bodies in plasma samples. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Jahr et al. and Mok et al. because the microarray technology would allow a potential screening method to detect increased levels of nucleic acids of apoptotic bodies in plasma samples with a high throughput.

Conclusion

19. Claims 10-14, 23, 25 and 27 are rejected.

20. Claims 15, 18, 19, and 20 are objected to for depending from rejected claims.

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meera Natarajan whose telephone number is 571-270-3058. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER